Dear editor/reviewers,

Thank you very much for your valuable comments. Revision has been made in the original manuscript according to your advice and the revised portions were marked in yellow background. We will respond to each point as listed below. Hope these will make it more acceptable for publication. Thanks again!

Reviewer 1

1. Authors may put the univariate and multivariate results, as shown in Table 2, into their discussion. As the other studies do, the predictors are most related to male, Black, older age, poorly differentiated, without chemotherapy, etc. They analyzed that location at rectum had better outcome but this may not be true for colon without discussion for sidedness.

Response:

The univariate and multivariate results have been added into the discussion. With respect to tumor location, other studies were cited and their results were in line with our findings.

2. The most part I have concerned is that the SEER data is belonged to a registered institute in U.S. and whether there is any ethic issue or not. I cannot find any related documented file in your attached. Isn't it too strange that the US patients' data was reported by a hospital outside the US? Unless your hospital patients also involved in the study or you have been authorized by the SEER.

Response:

SEER is an open public database for every researcher in the world. Written informed consent is not needed. Many articles have been published based on the SEER. For example, PMID: 30138618 was from Japan, PMID: 30220604 was from China, PMID: 26857456 was from many parts of the world.

Reviewer 2

1. The authors divided the patients into two groups, over 65 and under. The authors should explain what criteria they have done. In my opinion, it is best to do this with ROC curve analysis.

Response:

Thank you very much for your comments. The criteria should be added indeed. But we don't know how to use ROC curve analysis to determine the cutoff value. Alternatively, we used the X-tile program. The following words were added in the Method section: "Patients were divided into two groups based on the median age and calculation result of X-tile program (Yale University, 3.6.1, Figure S1)." The median age was 63. The cutoff value determined by X-tile ranged from 61 to 77. So we used 65 as the optimal cutoff value.

2. Is the data in Table-2 related to propensity score matching groups? or is it related to all patients mentioned in Table-1? In other words, if propensity

score matching will be used, there is no need for statistics in Table-1. Only descriptive features should be given in Table-1.

Response:

Table-2 was related to propensity score matching groups. Table-1 showed the descriptive features of entire cohort.

Reviewer 3

1. Immediate chemotherapy following endoscopic colorectal stent may bring better outcome as compared to primary tumor resection.

Response:

Immediate chemotherapy following endoscopic colorectal stent means they will not receive any palliative surgery afterwards? Then this segment of patients is classified as “no surgery” in our study. Unfortunately, SEER doesn’t provide information about the sequence of chemotherapy and surgery. There is no way to differentiate between neoadjuvant chemotherapy and adjuvant chemotherapy. We are very sorry.

2. We may want to know what are the other positive prognostic factors in addition to lung M1a metastases after palliative primary resection, e.g., RAS wild type, primary resection after chemotherapy rather than upfront resection, etc.

Response:

SEER doesn’t provide information about RAS status or the sequence of

chemotherapy and surgery. We don't know whether patients receive chemotherapy before or after surgery. We are very sorry.

3. The selection criteria. (5) no previous surgery for metastatic site. The authors do not seem to show whether conversion M1a diseases were included or not. Were not there any patients, e.g., who underwent R0 liver resection after palliative primary resection followed by chemotherapy as conversion diseases?

Response:

Thank you very much for your comments. Patients who underwent R0 liver resection were excluded. If there are any surgery records about metastatic site (including distant lymph nodes) in the SEER, the patient will be excluded. We deleted the word "previous" so that it would not be confusing.

4. Did not the patients analyzed in the present study, 2935 M1a diseases and 2145 M1b disease, undergo any surgical procedure through the clinical courses?

Response:

No, this is not the case. PSM will automatically match similar patients based on some algorithm in order to adjust potential confounding variables and decrease selection bias. As a result, 2935 M1a diseases and 2145 M1b disease can't be matched to similar patients and then they are excluded. For example, a patient aged 100 received surgery. No patient with similar age (100 or 98 yrs or something similar) received surgery, and this patient will

be excluded in the PSM.

5. When did the patients undergo primary resection? Did all patients undergo an upfront surgery or a resection during palliative chemotherapy?

Response:

SEER doesn't provide information about the sequence of chemotherapy and surgery. We are very sorry for this. We can't identify the time. They may undergo an upfront surgery or a resection during palliative chemotherapy. The only thing we can be sure of is that they undergo surgery.

6. Why did not the authors show the data divided by colon and rectum, individually? Palliative primary resection seems to have a risk of anastomotic leak after lower rectal cancer.

Response:

Actually, we did this in private. Not only that, we divided colon into right colon and left colon. Similar results were observed (M1a gained more benefits than M1b). The aim of the study is to examine whether there is difference between the prognosis of M1a and M1b receiving palliative primary tumor resection. Since both colon and rectum share the same AJCC TNM staging system (M1a and M1b), to our way of thinking, there's no need to differentiate them. Thank you very much!

7. Did the present study include patients undergoing colorectal endoscopic stent to prevent obstruction or bleeding in the present study? Indeed, many

CRA patients with unresectable metastatic diseases can be treated with immediate chemotherapy after colorectal stent.

Response:

We are sorry for this. SEER doesn't provide information about colorectal endoscopic stent. It only provides basic information like age, sex, surgery or not, chemotherapy or not. There is no further detailed information.

8. The authors did not show RAS and BRAF status of the tumor. How does the wild type group or mutation group affect the survival period concerning palliative chemotherapy?

Response:

We are very sorry for this. SEER doesn't provide information about gene information.